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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/691,343 | 10/18/2000 | C. Alexander Turner JR. | LEX-0070-USA | 3960 |

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| EXAMINER |
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DEBERRY, REGINA M

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| ART UNIT | PAPER NUMBER |
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1647

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/691,343

Applicant(s)

TURNER ET AL.

Examiner

Regina M. DeBerry

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- ☐ Interview Summary (PTO-413) Paper No(s). _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other:

Status of Application, Amendments and/or Claims

The amendment filed 11 March 2003 (Paper No. 13) has been entered in full. New claims 9-11 were added. Claims 4-11 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claim 5 under 35 USC 112, first paragraph, written description as set forth at pages 7-9 of the previous Office Action (06 November 2002, Paper No. 11) is *withdrawn* in view of the amendment (11 March 2003, Paper No. 13).

The rejection of claim 5 under 35 USC 112, second paragraph as set forth at pages 9-10 of the previous Office Action (06 November 2002, Paper No. 11) is *withdrawn* in view of the amendment (11 March 2003, Paper No. 13).

Claim Rejections - 35 USC § 101

Claims 4-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. The basis for this rejection is set forth at pages 3-5 of the previous Office Action (06 November 2002, Paper No. 11).

Applicant states that the present invention has a number of substantial and credible utilities, not the least of which is in diagnostic assays, as described in the specification. The present sequence defines a coding single nucleotide polymorphism- specifically, an A/T polymorphism at position 598 of SEQ ID NO:6, which can lead to an

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isoleucine or valine residue at amino acid position 200 of SEQ ID NO:7. Applicant contends that polymorphisms are the basic for diagnostic assays such as forensic analysis, which is undoubtedly a real world utility, the present sequences must in themselves be useful. Applicant states that it is important to note that the presence of more useful polymorphic markers for forensic analysis would not mean that the present sequence lack utility.

Applicant's arguments have been fully considered but not deemed persuasive. The specification states "the described open reading frames *can* also contain a polymorphism including an *A to G transition* at base 598 of SEQ ID NO:6 which converts isoleucine at position 200 of SEQ ID NO:7 to a valine". Thus the gene does not necessarily contain a polymorphism. Even if the gene contained single nucleotide polymorphisms, it does not mean that the change in amino acid will affect activity or cause a disease or condition. Furthermore, the invention could not be used in a diagnostic assay because the protein does not have a known function or mechanism to assay. It is known that the utility of a claimed DNA does not necessarily depend on the function of the encoded gene product, if the claimed DNA had a specific and substantial utility such as it hybridizes near a disease-associated gene or it has a gene regulating activity. The specification, however, fails to disclose that the DNA of the instant application can be linked to a specific disease or gene regulating activity.

Applicant states that four sequences sharing 100% identity at the protein level over an extended region of the claimed sequence are present in the leading scientific repository for biological sequence data and have been annotated by scientists as homo

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sapiens platelet derived growth factor C. Applicant maintains, given the GenBank annotations, there can be no question that those skilled in the art would clearly believe that Applicant's sequence is a platelet derived growth factor, as described in the specification as originally filed.

Applicant's arguments have been fully considered but not deemed persuasive. The sequence alignment demonstrates 100% sequence identity with 234 out of 305 amino acid residues of (SEQ ID NO:7) and 234 out of 345 amino acid residues of PDGF-C. Li *et al.* (abstract submitted by Applicant, Exhibit C), teach the primary structure of human PDGF-C. For example three putative N-linked glycosylation sites are located at positions 22, 55 and **254** (page 302, 4th paragraph). The core region of PDGF-C (PDGF-CC) which contains only the PDGF/VEGF domain comprises residues **230-345**. The core domain of PDGF-C but not the full length protein, efficiently competed with PDGF-BB for binding to PDGFR- β and PDFG-AA for binding to PDGFR- α (pages 303, 4th paragraph). PDGF-CC induces tyrosine phosphorylation of PDGFR- α and induces cellular DNA synthesis mediated by PDGFR- α (page 304). Li *et al.* teach a polypeptide sequence of 345 amino acids. Li *et al.* teach that the PDGF-C protein is synthesized and secreted as a latent growth factor, requiring proteolytic removal of the N-terminal CUB domain for receptor binding and activation (page 307, 3rd paragraph). The activity is of PDGF-C protein (core domain) is residues 230-345. The instant specification does not teach the full length PDGF-C protein. The instant specification teaches residues 1-305 (SEQ ID NO:7) only 1-234 residues of SEQ ID NO:7 share 100% sequence identity with the PDGF-C protein. Thus, the polypeptide

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taught by the specification will not have activity as taught by Li et al. and it is not clear how a protein devoid of activity will have utility.

Applicant states that the Skolnick reference cited by the Examiner is not applicable because it concerns prediction of function based on the presence of certain functional motifs present within a give protein sequence. Applicant states that the Tischer reference hardly represents the view of those skilled in the art at the time of the present application regarding the prediction of protein function based on homology. Applicant states that the different receptors bound by the two isoforms are in fact related (Yan *et al.*). Applicant's arguments are not deemed persuasive. The specification states, "this NHP, described for the first time herein, shares structural similarity with animal proteins that contain CUB domains". "The CUB domain is an extracellular domain protein in a variety of diverse proteins" (page 2, lines 25-31 and page 7, lines 29-37)). Contrary to Applicant's assertion, predictions on function were also made based on the presence of certain functional motifs or structures. The age of the Tischer reference does not take away from the fact that there are circumstances where individual members of a protein family can have distinct and sometimes opposite, biological activities. The Yan *et al.* reference was cited to show that EDA-A1 and EDA-2, while being members of the tumor necrosis factor family, are differentially expressed, bind different receptors and may have distinct roles in development of the hair follicle.

Applicant contends that SEQ ID NO:6 can be used to map the 5 coding exons on chromosome 4. The polynucleotide provides specificity in localizing the specific region

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of the human chromosome 4 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequence. This is not found persuasive because mapping a region on chromosome 4 is not specific to the instant invention. Any chromosome region 4 gene can be used to map that particular area of the chromosome.

Applicant cites case law to demonstrate utility of the instant invention. However, some of the cases are not applicable to the rejection. For example, Applicant cites *Brooktree Corp. v. Advanced Micro Devices, Inc.* 24 USPQ 29 1401, 1412 (Fed Cir. 1992). However, this case involves patent infringement involving semiconductor chips used in color video displays. The validity of the patent was challenged. "If the claimed subject matter is inoperable, the patent may indeed be invalid for failure to meet the utility requirement of Section 101 and the enablement requirement of Section 112". "To violate Section 101, the claimed device must be totally incapable of achieving a useful result". It is unclear to the Examiner, how this case is applicable to the argument at hand. The issue in this rejection is not an issue of inoperativeness. Rather, the rejection is based on the conclusion that the specification fails to provide a specific and substantial asserted utility or a well established utility. Contrary to Applicant's assertion, the Examiner is not confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a drug, nor is the Examiner confusing utility with enablement. The instant specification is not supported by a specific and substantial asserted utility or a well established utility for the reasons stated in the last Office Action. Indeed, a PDGF-C protein would have utility, however,

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the specification does not teach the full length sequence of PDGF-C polypeptide or the core domain sequence of PDGF-C which is taught by Li *et al.* to have activity. As was stated above, it is not clear how a protein devoid of activity would have utility.

The current rejection is in compliance with the most currently published version of the Utility Guidelines which require that all biological inventions must have credible, specific and substantial utility. Additionally, each Patent Application is examined on its own merits, what was deemed allowable in one Patent has no bearing on this Application. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 4-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pages 5-7 of the previous Office Action (06 November 2002, Paper No. 11).

Applicant incorporates their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicants arguments have been fully considered but are not found persuasive for the reasons discussed above in the maintained rejection under 35 USC 101.

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In addition, the specification is not enabled for fragments of polynucleotides (claims 4, 7 and 8 which read on fragments). Applicant states that there is no requirement that all species of an invention must have all of the exact same properties. Applicant maintains that it is well established that the enablement requirement is met if the description enables any mode of making and using the invention. Applicant states that there is sufficient knowledge and technical skill in the art for a skilled artisan to be able to make and use the claimed DNA species in a number of different aspects of the invention entirely without further details in a patent specification. Applicant cites the oligonucleotide probes and primers, PCR based screening and detection methods. Applicant asserts that a patent need not disclose what is well known in the art. A specification need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it.

Applicant's arguments have been fully considered but are not found persuasive. There is no requirement that all species of an invention have the exact same properties. However, the rejected claims encompass fragments of NHP which do not have a property. The specification indicates that the polynucleotides are useful in that they encode a protein with a particular biological activity. The specification teaches NHP as a member of the platelet-derived growth factor/VEGF family of proteins. The specification teaches the NHP polypeptide as SEQ ID NO:7 (305 amino acid residues). Claim 4 reads on an isolated nucleic molecule comprising *at least 24* contiguous bases in SEQ ID NO:7. The expressed protein could have about 8 or 9 amino acids residues (claims 7 and 8). There is no assurance that when the DNA is expressed, the protein would have

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the desirable properties of the invention. The specification does not teach how to use an inactive NHP protein. Furthermore, the specification does not teach how to make a fragment of NHP while still maintaining the activity sought to be patented. The specification has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. If one skilled in the art can readily anticipate the effect, then there is predictability in the art. In this case, there is high unpredictability. The references submitted by the Examiner establish the unpredictability of the effects of mutation on protein structure and function. Without sufficient guidance, the changes which can be made in the structure and still maintain sufficient activity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. Lastly, fragment of polynucleotides often have less specificity than the full length sequence. The polynucleotide fragment may correspond to a region that is highly conserved in a gene family or unrelated DNA sequences. The specification does not teach how to make and/or use other sequences which may cross hybridize with the instant invention. Thus the scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pages 5-7 of the previous Office Action (06 November 2002, Paper No. 11).

Applicant cites case law to demonstrate written description for the instant claim. Applicant states that using the nucleic and amino acid sequences of the present invention, the skilled artisan would readily be able to distinguish the claimed nucleic acids from other material on the basis of the specific structural provides. Applicant's arguments have been considered but are not found persuasive. There is substantial variability among the species of DNAs encompassed within the scope of the claims that is not described. Polynucleotides comprising at least 24 contiguous nucleotides from the nucleotide sequence of SEQ ID NO:6 read on fragments of SEQ ID NO:1. The specification discloses only a structural feature of SEQ ID NO:1. The claim encompasses genes yet to be discovered. The genes could be unrelated DNA sequences, corresponding sequences from other species, mutated sequences, allelic variants, splice variants and so forth. The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The disclosure fails to provide a representative

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number of species to describe the genus. Applicant's argument has failed to overcome the 35 USC 112, first paragraph written description rejection.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

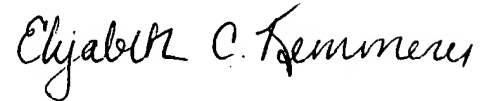
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



RMD
June 10, 2003



ELIZABETH KEMMERER
PRIMARY EXAMINER